CROSS-REFERENCE

This application is a Continuation-In-Part of U.S. Patent Application Serial No. 09/855,468 filed May 15, 2001, ~~now pending~~ now abandoned and of International Patent Application No. PCT/US00/18777 having an international filing date of 10 July, 2000, now pending.

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RESEARCH SUPPORT

The research for the present invention was supported in part by grants from the Multiple Sclerosis Society of Canada and the Canadian Myelin Research Initiative.

FIELD OF THE INVENTION

The present invention is concerned generally with glial cell components of the central nervous system; and is particularly directed to in-vitro isolation of embryonic human microglia ("HM") cells and establishment of immortalized human microglia ("HMO6") cells and cell lines which are identifiable, stable, functionally active, and in continuous proliferation in-vitro.

BACKGROUND OF THE INVENTION

Microglia are a major glial component of the central nervous system (CNS); play a critical role as resident immunocompetent cells and phagocytic cells in the CNS [van Furth,

For these reasons, a variety of in-vitro assays and in-vivo therapeutic uses are envisioned and intended for the present invention. These include the following:

1. The immortalized human microglia cells can be used in-vitro to isolate neurotoxic or neurotrophic molecules naturally produced by human microglia or produced in response to inflammatory factors or neuroactive molecules such as β-~~amyloid.~~ amyloid

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2. Because microglia have been implicated in neurological disorders, such as Alzheimer disease, Parkinson disease, AIDS-dementia, ALS and MS, the immortalized human microglia can be used for discovery (screening) of new drugs to treat the aforementioned conditions and inflammation. Prospective drug candidates are those that can counter or reduce production of proinflammatory cytokines, oxygen radicals, proteases such as caspase-3 and -8, and neurotoxic agents such as β-amyloid.

3. Human immortalized microglial cells can be further genetically manipulated to express and produce additional proteins, peptides, or prodrugs. Such substances would include a diverse range of chemokines, cytokines, and various marker proteins (e.g., LacZ and GFP), growth factors, neurotrophic molecules, anti-apoptotic molecules (e.g., Bcl-2), and enzyme inhibitors (e.g., caspase inhibitor). Microglia cells can be additionally genetically modified to block the production of proteins that typically become overproduced by nervous system pathologies. For example, upstream from the v-myc gene, there can be inserted an activatable suppressor gene. Alternately, for human treatment, there can be inserted a suicide gene.